DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
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Silver Spring, MD 20993-0002

October 17, 2014

ROCHE DIAGNOSTICS
KELLI TURNER
U.S. REGULATORY AFFAIRS PRINCIPAL
9115 HAGUE ROAD
INDIANAPOLIS IN 46250-0416

Re: K141426
Trade/Device Name: Elecsys Folate III
Regulation Number: 21 CFR 862.1295
Regulation Name: Folic acid test system
Regulatory Class: II
Product Code: CGN
Dated: September 10, 2014
Received: September 11, 2014

Dear Ms. Turner:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Courtney H. Lias -S

Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
k141426

Device Name
Elecsys Folate III

Indications for Use *(Describe)*
Binding assay for the in vitro quantitative determination of folate in human serum. The binding assay is intended for use on Elecsys and cobas e immunoassay analyzers. Folic acid measurements are used in the diagnosis and treatment of anemias.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON A SEPARATE PAGE IF NEEDED.

FOR FDA USE ONLY

Concurrence of Center for Devices and Radiological Health (CDRH) *(Signature)*

510(k) Summary for the Elecsys Folate III Assay

Introduction

According to the requirements of 21 CFR 807.92, the following information provides sufficient detail to understand the basis for a determination of substantial equivalence.

Submitter Name, Address, Contact

Roche Diagnostics
9115 Hague Road
P.O. Box 50416
Indianapolis, IN 46250-0415

Contact Person: Kelli Turner

- Phone: (317) 521-4515
- Fax: (317) 521-2324
- Email: kelli.turner@roche.com

Date Prepared: October 9, 2014

Purpose

In accordance with 21 CFR 807.87, Roche Diagnostics hereby submits official notification as required by Section 510(k) of the Federal Food, Drug and Cosmetics Act of our intention to market the device described in this Premarket Notification [510(k)].

The purpose of this premarket notification is to obtain FDA review and clearance for the Folate III Assay.

Device Name

Proprietary name:	Elecsys Folate III Assay
Common name:	Folate III assay
Classification name:	Acid, Folic, Radioassay
Product Code:	CGN
Predicate Device:	Roche Elecsys Folate III (k082340)

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510(k) Summary for Elecsys Folate III Assay, *continued*

Establishment Registration

For the Elecsys Folate III assay, the establishment registration number for Roche Diagnostics GmbH in Mannheim, Germany, is 9610126 and for Penzberg, Germany, is 9610529. The establishment registration number for Roche Diagnostics in the United States is 1823260

Classification

The FDA has classified the Radiometry, Folate III assay as a Class II device.

Device Description

The Folate III Assay employs a competitive test principle using natural folate binding protein (FBP) specific for folate. Folate in the sample competes with the added folate (labeled with biotin) for the binding sites on FBP (labeled with a ruthenium complex).

Results are determined using a calibration curve that is generated specifically on each instrument by a 2 point calibration and a master curve (5-point-calibration) provided with the reagent bar code.

Reagents-working solutions	Description	Volume
PT1: Pretreatment reagent 1	Sodium 2-mercaptoethanesulfonate (MESNA) 40 g/L, pH 5.5	4 mL
PT2: Pretreatment reagent 2	Sodium hydroxide 25 g/L	5 mL
M: Microparticle	Streptavidin-coated microparticles 0.72 mg/mL; preservative	6.5 mL
R1: Folate binding protein	Ruthenium labeled folate binding protein 75 µg/mL; human serum albumin (stabilizer); borate/phosphate/citrate buffer 70 mmol/L, pH 5.5; preservative	9 mL
R2: Folate~biotin	Biotinylated folate 17 µg/L; biotin 120 µg/L; human serum albumin (stabilizer); borate buffer 100 mmol/L, pH 9.0; preservative	8 mL

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510(k) Summary for Elecsys Folate III Assay, *continued*

Intended Use/ Indications for Use

Elecsys Folate III:

Binding assay for the in vitro quantitative determination of folate in human serum. The binding assay is intended for use on Elecsys and **cobas e** immunoassay analyzers. Folic acid measurements are used in the diagnosis and treatment of anemias.

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Substantial Equivalence

The Elecsys Folate III assay is substantially equivalent to other devices legally marketed in the United States.

The Elecsys Folate III assay is equivalent to Elecsys Folate III assay (k082340).

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510(k) Summary for Elecsys Folate III Assay, *continued*

Substantial Equivalence - Comparison

The following table compares the Elecsys Folate III Assay with its predicate device (k082340).

Comparison of Assays, Similarities and Differences

Table 1

Assay Comparison		
Feature	**Predicate Device: Roche Elecsys Folate III (k082340)**	**Candidate Device: Elecsys Folate III Assay**
General Assay Features		
Intended Use/ Indications for Use	Intended for the in vitro quantitative determination of folate in human serum. The binding assay is intended for use on Elecsys and **cobas e** immunoassay analyzers.	Same.
Assay Protocol	The Elecsys Folate assay employs a competitive test principle using natural folate binding protein (FBP) specific for folate. Folate in the sample competes with the added folate (labeled with biotin) for the binding sites on FBP (labeled with ruthenium).	Same.
Detection Protocol	Electrochemiluminescent Assay	Same.
Applications	27-minute application	Same.
Instrument Platform	Elecsys and cobas e immunoassay analyzers.	Same.
Sample Volume	25 µL	Same
Sample Type	Human serum.	Same.

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510(k) Summary for Elecsys Folate III Assay, *continued*

Comparison of Assays—Similarities and Differences, *continued*

Table 1 ***continued***

Assay Comparison		
Feature	**Predicate Device: Roche Elecsys Folate III (k082340)**	**Candidate Device: Elecsys Folate III Assay**
General Assay Features		
Reagents	Competition principle. Total duration of assay: 27 minutes	Same.
Calibrator	Elecsys Folate III CalSet	Same.
Calibration Interval	Calibration must be performed once per reagent lot using fresh reagent (i.e. not more than 24 hours since the reagent kit was registered on the analyzer). Renewed calibration is recommended as follows: **cobas e 411** analyzers: • After 1 month (28 days) when using the same reagent lot. • After 7 days (when using the same reagent kit on the analyzer). As required: e.g. quality control findings outside the specified limits	Same.
Controls	Elecsys PreciControl Varia	Same.
Traceability /Standardization	Standardized against the Elecsys Folate II assay (k043318)	Standardized against WHO International Standard NIBSC code: 03/178.

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510(k) Summary for Elecsys Folate III Assay, *continued*

Comparison of Assays—Similarities and Differences, *continued*

Table 1 ***continued***

Assay Comparison		
Feature	**Predicate Device: Roche Elecsys Folate III (k082340)**	**Candidate Device: Elecsys Folate III Assay**
General Assay Features		
Reagent Stability	Unopened: 2-8°C - Up to the stated expiration date Opened 2-8°C - 8 weeks On Analyzers – 2 weeks or 4 weeks when stored altermatively in the refrigerator and on the analyzer, with the toal time on-board the analyzer not exceeding 10x8 hours	Same.
Measuring Range	1.50– 20.0 ng/mL	2.0- 20.0 ng/mL
Analytical Sensitivity	Limit of Blank (LoB): = 0.640 ng/mL Limit of Detection (LoD): = 1.50 ng/mL Limit of Quantitation (LoQ): = 2.0 ng/mL	Limit of Blank (LoB): = 0.6 ng/mL Limit of Detection (LoD): = 1.2 ng/mL Limit of Quantitation (LoQ): = 2.0 ng/mL
Analytical Specificity	Cross reactant / concentration tested (ng/mL) / Highest cross-reactivity observed (%) Amethopterin / 750 / 2.3 Aminopterin / 750 / 2.7 Folonic acid / 750 / 2.3	Cross reactant / concentration tested (ng/mL) / Highest cross-reactivity observed (%) Amethopterin / 1500 / 2.5 Aminopterin / 1500 / 4.4 Folonic acid / 1500 / 0.7

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510(k) Summary for Elecsys Folate III Assay, *continued*

Comparison of Assays—Similarities and Differences, continued

Table 1 *continued*

Assay Comparison		
Feature	**Predicate Device: Roche Elecsys Folate III (k082340)**	**Candidate Device: Elecsys Folate III Assay**
Labeled Performance Characteristics		
Precision	***cobas e** 411:* Within-run Sample / Mean / SD / CV HS 1 4.30 0.157 3.7% HS 2 6.17 0.274 4.4% HS 3 6.83 0.288 4.2% HS 4 15.7 0.620 4.0% PCV1 4.05 0.235 5.8% PCV2 11.8 0.562 4.8% Total Sample / Mean / SD / CV HS 1 4.30 0.383 8.9% HS 2 6.17 0.444 7.2% HS 3 6.83 0.484 7.1% HS 4 15.7 0.956 6.1% PCV1 4.05 0.382 9.4% PCV2 11.8 0.845 7.2%	***cobas** e 411:* Within-run (will be labeled Repeatability) Sample / Mean / SD / CV HS 1 2.29 0.155 6.8% HS 2 3.92 0.200 5.1% HS 3 11.9 0.346 2.9% HS 4 13.4 0.301 2.2% HS 5 17.8 0.44 2.5% PCV1 3.24 0.215 6.6% PCV2 11.6 0.314 2.7% Total (will be labeled Intermediate) Sample / Mean / SD / CV HS 1 2.29 0.247 10.8% HS 2 3.92 0.318 8.1% HS 3 11.9 0.571 4.8% HS 4 13.4 0.574 4.3% HS 5 17.8 0.67 3.7% PCV1 3.24 0.309 9.5% PCV2 11.6 0.566 4.9%

HS= Human Serum
PCV1=PreciControl Varia level 1
PCV2=PreciControl Varia level 2

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510(k) Summary for the Elecsys Folate III Assay, *continued*

Table 1 *continued*

Assay Comparison		
Feature	**Predicate Device: Roche Elecsys Folate III (k082340)**	**Candidate Device: Elecsys Folate III Assay**
Labeled Performance Characteristics		
Limitations	The assay is unaffected by: • Bilirubin < 33 mg/dL • Lipemia < 1500 mg/dL • Biotin < 21 ng/mL • Rheumatoid factors < 1000 IU/mL • IgG < 1.6 g/dL • IgA < 0.4 g/dL • In vitro tests were performed on 18 commonly used pharmaceuticals and in addition on human erythropoeetin. No interference with the assay was found. • Samples with extremely high total protein concentrations (e.g. patients suffering from Waldenstrom's macroglobulinemia) are not for use in this assay. • In rare cases, interference due to extremely high titers of antibodies to analyte-specific antibodies, streptavidin or ruthenium can occur. These effects are minimized by suitable test design. • It is contraindicated to measure samples of patients receiving therapy with certain pharmaceuticals, e.g. methotrexate or leucovorin, because of the cross-reactivity of folate binding protein with these compounds. For diagnostic purposes, the results should always be assessed in conjunction with RBC folate, the patient's medical history, clinical examination and other findings.	The assay is unaffected by: • Bilirubin < 29 mg/dL • Lipemia < 1500 mg/dL • Biotin < 21 ng/mL • Rheumatoid factors < 1000 IU/mL • IgG < 1.6 g/dL • IgM < 1.0 g/dL • IgA < 0.4 g/dL • In vitro tests were performed on 16 commonly used pharmaceuticals and in addition on human erythropoeetin. No interference with the assay was found. • Samples with extremely high total protein concentrations (e.g. patients suffering from Waldenstrom's macroglobulinemia) are not for use in this assay. • In rare cases, interference due to extremely high titers of antibodies to analyte-specific antibodies, streptavidin or ruthenium can occur. These effects are minimized by suitable test design. • It is contraindicated to measure samples of patients receiving therapy with certain pharmaceuticals, e.g. methotrexate or leucovorin, because of the cross-reactivity of folate binding protein with these compounds. For diagnostic purposes, the results should always be assessed in conjunction with RBC folate, the patient's medical history, clinical examination and other findings.

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510(k) Summary for the Elecsys Folate III Assay, *continued*

Comparison of Assays—Similarities and Differences, continued

Table 1 *continued*

<table>
<tr><th colspan="3">Assay Comparison</th></tr>
<tr><th>Feature</th><th>Predicate Device: Roche Elecsys Folate III (k082340)</th><th>Candidate Device: Elecsys Folate III Assay</th></tr>
<tr><th colspan="3">Labeled Performance Characteristics</th></tr>
<tr><td>Reference range study</td><td>
<table>
<tr><td>Country</td><td>(N)</td><td colspan="2">Median</td><td colspan="2">2.5th-97.5th percentile</td></tr>
<tr><td rowspan="2">USA</td><td rowspan="2">261</td><td>nmol/L</td><td>ng/mL</td><td>nmol/L</td><td>ng/mL</td></tr>
<tr><td>31.8</td><td>14.0</td><td>16.6-59.3</td><td>7.3-26.1</td></tr>
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<table>
<tr><td>Country</td><td>(N)</td><td colspan="2">Median</td><td colspan="2">2.5th-97.5th percentile</td></tr>
<tr><td rowspan="2">USA</td><td rowspan="2">214</td><td>nmol/L</td><td>ng/mL</td><td>nmol/L</td><td>ng/mL</td></tr>
<tr><td>26.8</td><td>11.8</td><td>10.9-54.9</td><td>4.78-24.2</td></tr>
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</td></tr>
<tr><th>Feature</th><th>Predicate Device: Abbott Architect Folate assay (k092740)</th><th>Candidate Device: Elecsys Folate III Assay</th></tr>
<tr><td>Method Comparison</td><td colspan="2">
<table>
<tr><td>n = 106
Min = 2.08 ng/mL
Max = 19.6 ng/mL</td><td>Passing/Bablok</td><td>Linear regression</td></tr>
<tr><td>Slope</td><td>0.980</td><td>0.976</td></tr>
<tr><td>Intercept</td><td>-0.095</td><td>0.041</td></tr>
<tr><td>Tau/r</td><td>0.924</td><td>0.984</td></tr>
<tr><td>Bias at 4 ng/mL</td><td>-0.175</td><td>-0.054</td></tr>
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510(k) Summary for the Elecsys Folate III Assay, *continued*

Standard/ Guidance Document Reference

In addition to FDA guidance regarding 510(k) submissions, the following standards were used for the performance studies.

- Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline – Second Edition. CLSI document EP5-A2, Volume 24, No. 25, August 2004.

- Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline- Second Edition. CLSI document EP17-A2, Volume 32, No. 8, June 2012

- Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline. CLSI document EP6-A, Volume 23, No. 16, April 2003.

- Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline; Approved Guideline. CLSI document EP-09-A2-IR, Volume 22, No. 19, September 2002

Conclusion

The submitted information in this premarket notification supports a substantial equivalence decision. The data supports a safe, effective device which performs as well as or better than the predicate device.